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Analysis of Deterministic and Stochastic HIV Models

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Abstract

In this research paper, I apply the Susceptible-Infected-Virus (SIV) model to the Human Immunodeficiency Virus (HIV). The SIV model is a compartmental model describing within-host dynamics of viral infections; I analyze it in both its deterministic (in which constants are assumed to be known exactly) and stochastic (in which the death rate of the healthy cells is represented by a random variable) forms. First, I give analytical solutions to two simplified versions of the deterministic model. Next, I apply numerical methods to the full deterministic and stochastic systems. The results give an illustrative picture of HIV in-host population dynamics in the absence of treatment. They also demonstrate how randomness can impact the progression of the disease.

1 The Susceptible-Infected-Virus Model

The Susceptible-Infected-Virus (SIV) model is a system of ordinary differential equations that describes the interaction of virus particles with the cells of a living organism. We apply the SIV model to the human immunodeficiency virus (HIV). To begin, it will be useful to outline the basic concepts of virus-cell dynamics, which are described in more detail in [9]. A virus is essentially genetic material enclosed in a protein shell. The virus particle enters an organism and then infects a cell by attaching to the cell wall and inserting its genetic material, either DNA or RNA. This genetic material makes its way to the cell's nucleus and reprograms the cell to make copies of the virus. After many copies have been made, the cell undergoes either bursting or budding, releasing new virus particles that can go on to infect other cells. In the case of HIV, the new viruses are released through the budding process, so that the infected cell remains intact. The cells targeted by HIV are CD4+ T-cells, which are helper cells that aid in immune system responses. In simple terms, HIV impairs the body's ability to fight off viruses and bacteria.

Various HIV models and their properties have been studied. The most common is the basic model of virus dynamics (SIV model), given by

$$\frac{dS}{dt} = \lambda - dS - kVS, \tag{1}$$

$$\frac{dI}{dt} = kVS - \delta I, \tag{2}$$

$$\frac{dV}{dt} = N_T \delta I - cV, \tag{3}$$

where S is the number of healthy cells, I is the number of infected cells, and V is the number of free virus particles. The other symbols (λ, d, k, δ, N_T, and c) are positive constants. Approximations for their values (obtained from [9]) are given in Table 1.

Parameter	Value	Units	Description
λ	0.1089	cells/day	Healthy T-cell Growth Rate
d	0.01089	1/day	Healthy T-cell Death Rate Constant
k	1.179×10^{-3}	1/(virions·day)	Infection Rate Constant
δ	0.3660	1/day	Infected Cell Death Rate Constant
N_T	4246.4	virions/cell	Virus Production Rate Constant (per infected cell)
c	3.074	1/day	Viral Clearance Rate Constant

Table 1: Values of Constants (obtained from [9])

It is worth taking a moment to discuss the biological meanings of the terms in Equations (1)-(3). As previously mentioned, S represents the number of healthy T-cells present in a patient's blood (per cubic milliliter) at any given time, I represents the number of infected cells, and V is the number of free virus particles. Examining Equation (1), the first term is λ, which represents the birth rate for healthy T-cells. The second term, $-dS$, represents the healthy cell death rate. Finally, $-kVS$ represents the rate at which healthy cells are infected by virus particles. Looking at Equation (2), the term kVS appears again, but this time it is positive. This makes sense since, once a virus particle infects a healthy cell, it becomes an infected cell. The term $-\delta I$ represents the death rate for the infected cells. Lastly, in the third equation, $Nt\delta I$ is the viral production rate (the rate at which infected cells produce virus particles), and $-cV$ is the viral clearance rate (the rate at which virus particles are removed from the body).

In this paper, we analyze both deterministic and stochastic versions of this model. The deterministic system is analyzed in Chapter 2, first showing the existence and uniqueness of a solution and finding the equilibria. Next, two simplified versions of the SIV model are solved analytically, and the full model is solved using numerical methods. Chapter 3 investigates a stochastic version of the model, replacing the constant d with a random variable. First, basic probability concepts are introduced, followed by a discussion of the existence and uniqueness of a solution, and finally ending with the use of numerical methods to find the expectation and variance of the solution.

2 The Deterministic Model

2.1 Existence and Uniqueness of Solutions

Our goal is to prove the Picard-Lindelöf Theorem and then apply it to the SIV model. To begin, we introduce a few basic concepts on metric spaces, obtained from [8], ending with a proof of the Contraction Mapping Theorem. Afterwards, the Picard-Lindelöf Theorem is used to show that the SIV model has a unique solution.

2.1.1 Introduction to Metric Spaces

Definition 2.1. *A metric space is a set A together with a function $\rho : A \times A \to \mathbb{R}$, $\rho(x, y)$ being called the distance from x to y, such that*

1. *$\rho(x, y) > 0$ if $x \neq y$, and $\rho(x, x) = 0$;*
2. *$\rho(x, y) = \rho(y, x)$ for all $x, y \in A$;*
3. *$\rho(x, z) \leq \rho(x, y) + \rho(y, z)$ for all $x, y, z \in A$.*

Example 2.2. *For any $n \in \mathbb{N}$, $\mathbb{R}^n$ is a metric space. Let $\boldsymbol{x} = (x_1, \ldots, x_n)$ and $\boldsymbol{y} = (y_1, \ldots, y_n)$ be elements of $\mathbb{R}^n$. Define the Euclidean norm by*

$$||\boldsymbol{x}|| = \left(\sum_{i=1}^{n} x_i^2 \right)^{1/2},$$

and define the distance function by

$$d(\boldsymbol{x}, \boldsymbol{y}) = ||\boldsymbol{x} - \boldsymbol{y}|| = \left(\sum_{i=1}^{n} (x_i - y_i)^2 \right)^{1/2}.$$

It is easy to see that 1 and 2 in Definition 2.1 hold for d. To show 3, we will need the Cauchy-Schwarz inequality. Let $\lambda \in \mathbb{R}$ and $\boldsymbol{x}, \boldsymbol{y} \in \mathbb{R}^n$. We have

$$\begin{aligned} 0 \leq ||\lambda \boldsymbol{x} + \boldsymbol{y}|| &= \sum_{i=1}^{n} (\lambda x_i + y_i)^2 \\ &= \sum_{i=1}^{n} (\lambda^2 x_i^2 + 2\lambda x_i y_i + y_i^2) = \lambda^2 \sum_{i=1}^{n} x_i^2 + 2\lambda \sum_{i=1}^{n} x_i y_i + \sum_{i=1}^{n} y_i^2. \end{aligned}$$

In other words, the above quadratic polynomial in the real variable λ is non-negative, so either is has no roots, or it has one root of double multiplicity. It follows that the discriminant either negative or zero; that is,

$$4 \left(\sum_{i=1}^{n} x_i y_i \right)^2 - 4 \left(\sum_{i=1}^{n} x_i^2 \right) \left(\sum_{i=1}^{n} y_i^2 \right) \leq 0,$$

which implies

$$\left(\sum_{i=1}^{n} x_i y_i \right)^2 \leq \left(\sum_{i=1}^{n} x_i^2 \right) \left(\sum_{i=1}^{n} y_i^2 \right).$$

The above relationship, called the Cauchy-Schwarz inequality, holds for any two vectors $\boldsymbol{x}$ and $\boldsymbol{y}$. Now, let $\boldsymbol{x}, \boldsymbol{y}, \boldsymbol{z} \in \mathbb{R}^n$. We have

$$\begin{aligned} ||\boldsymbol{x} - \boldsymbol{z}||^2 &= ||\boldsymbol{x} - \boldsymbol{y} + \boldsymbol{y} - \boldsymbol{z}||^2 \\ &= \sum_{i=1}^{n} (x_i - y_i + y_i - z_i)^2 \\ &= \sum_{i=1}^{n} (x_i - y_i)^2 + 2 \sum_{i=1}^{n} (x_i - y_i)(y_i - z_i) + \sum_{i=1}^{n} (y_i - z_i)^2 \\ &\leq \sum_{i=1}^{n} (x_i - y_i)^2 + 2 \left(\sum_{i=1}^{n} (x_i - y_i)^2 \right)^{1/2} \left(\sum_{i=1}^{n} (y_i - z_i)^2 \right)^{1/2} + \sum_{i=1}^{n} (y_i - z_i)^2 \\ &= ||\boldsymbol{x} - \boldsymbol{y}||^2 + 2||\boldsymbol{x} - \boldsymbol{y}|| \cdot ||\boldsymbol{y} - \boldsymbol{z}|| + ||\boldsymbol{y} - \boldsymbol{z}||^2 \\ &= \left(||\boldsymbol{x} - \boldsymbol{y}|| + ||\boldsymbol{y} - \boldsymbol{z}|| \right)^2, \end{aligned}$$

or in other words, $d(\boldsymbol{x}, \boldsymbol{z}) \leq d(\boldsymbol{x}, \boldsymbol{y}) + d(\boldsymbol{y}, \boldsymbol{z})$. Hence, $\mathbb{R}^n$ with the distance function defined above is a metric space.

Definition 2.3. *If X and Y are metric spaces with metrics ρ_X and ρ_Y, respectively, then $f : X \to Y$ is continuous at $a \in X$ if for every $\epsilon > 0$ there is a $\delta > 0$ such that*

$$\rho_X(x, a) < \delta \quad \textit{implies} \quad \rho_Y(f(x), f(a)) < \epsilon.$$

Definition 2.4. *Let X and Y be metric spaces with metrics ρ_X and ρ_Y, respectively, and let $f : X \to Y$. We say that f is Lipschitz continuous if there exist constants c and r such that if $x_1, x_2 \in X$ and $\rho_X(x_1, x_2) < r$, then*

$$\rho_Y(f(x_1), f(x_2)) \leq c \rho_X(x_1, x_2).$$

Theorem 2.5. *Let X and Y be metric spaces and let $f : X \to Y$. If f is Lipschitz continuous, then f is continuous.*

Proof. Let X with metric ρ_X and Y with metric ρ_Y be metric spaces and let $f : X \to Y$ be Lipschitz continuous. Fix $x_1 \in X$, and let $\epsilon > 0$ be given. Since f is Lipschitz continuous, there exist constants c, r such that if $x_2 \in X$ and $\rho_X(x_1, x_2) < r$, then $\rho_Y(f(x_1), f(x_2)) \leq c\rho_X(x_1, x_2)$. Take $\delta = \min\{\epsilon/c, r\}$. Then, $\rho_X(x_1, x_2) < \delta \leq r$ implies

$$\rho_Y(f(x_1), f(x_2)) \leq c\rho_X(x_1, x_2) < c \cdot \delta \leq c \cdot \frac{\epsilon}{c} = \epsilon.$$

That is, if $\rho_X(x_1, x_2) < \delta$, then $\rho_Y(f(x_1), f(x_2)) < \epsilon$. Therefore, f is continuous at x_1. Since x_1 is arbitrary, f is continuous on X. □

Definition 2.6. *The (open) ball of radius r about p, $B_r(p)$ is defined by $B_r(p) = \{x : \rho(x, p) < r\}$.*

Definition 2.7. *A subset $A \subset X$ is open if every point p in A is the center of some ball included in A; that is, if for every $p \in A$, there exists $r > 0$ such that $B_r(p) \subset A$.*

Lemma 2.8. *Every ball is open; in fact, if $q \in B_r(p)$ and $\delta = r - \rho(p, q)$, then $B_\delta(q) \subset B_r(p)$.*

Proof. Let $B_r(p)$ be an open ball and let $q \in B_r(p)$. We must show that, for some $\delta > 0$, $B_\delta(q) \subset B_r(p)$. Let $\delta = r - \rho(p, q)$ and let $x \in B_\delta(q)$. By the Triangle Inequality (Definition 2.1.3),

$$\rho(x, p) \leq \rho(x, q) + \rho(q, p) < \delta + \rho(q, p) = r.$$

It follows that $x \in B_r(p)$. Therefore, since x was arbitrary, $B_\delta(q) \subset B_r(p)$. □

Definition 2.9. *A set A is closed if its complement A' (the set of all elements not in A) is open.*

Definition 2.10. *The union of all the open subsets of an arbitrary set A is called the interior of A and is designated A^{int}.*

Definition 2.11. *The closure, $\bar{A}$, of an arbitrary set A is the intersection of all closed sets including A. That is, $\bar{A}$ is the smallest closed set including A.*

Lemma 2.12. *For any set A, $(\bar{A})' = (A')^{int}$.*

Proof. Let A be a set. By Definition 2.11, $\bar{A} = \bigcap_j F_j$, where F_j is any closed set including A. By DeMorgan's Law,

$$(\bar{A})' = \left(\bigcap_j F_j\right)' = \bigcup_j F_j';$$

that is, $(\bar{A})'$ is the union of all open sets not including any part of A. By Definition 2.10, this is $(A')^{\text{int}}$. □

Lemma 2.13. *A point p is in $\bar{A}$ if and only if every ball about p intersects A.*

Proof. Let A be a set and let $p \notin \bar{A}$. By Lemma 2.12, this situation occurs if and only if $p \in (A')^{\text{int}}$. Equivalently, some ball about p does not intersect A. □

2.1.2 Sequential Convergence

Definition 2.14. *We say that the infinite sequence $\{x_n\}$ converges to the point a if for every $\epsilon > 0$, there is an $N \in \mathbb{N}$ such that $n > N$ implies $\rho(x_n, a) < \epsilon$. If this is the case, we write $x_n \to a$ as $n \to \infty$ or $\lim_{n\to\infty} x_n = a$.*

Theorem 2.15. *A point x is in the closure $\bar{A}$ of a set A if and only if there is a sequence $\{x_n\}$ in A converging to x.*

Proof. To prove the backward direction, let $\{x_n\}$ be a sequence in A that converges to x. Then any ball about x contains some x_n, so any ball about x intersects A. Hence $x \in \bar{A}$ by Lemma 2.13.

Now, to prove the forward direction, let $x \in \bar{A}$. Then, by Lemma 2.13, every ball about x intersects A. Then, taking $\delta_n = \dfrac{1}{n}$, we may choose $x_1 \in B_1(x) \cap A$, $x_2 \in B_{1/2}(x) \cap A$, and so on. Thus, we have found a sequence $\{x_n\}$ in A that converges to x. □

Theorem 2.16. *Let X and Y be metric spaces. A function $f : X \to Y$ is continuous at $a \in X$ if and only if, for any sequence $\{x_n\}$ in X, if x_n approaches a, then $f(x_n)$ approaches $f(a)$ as $n \to \infty$.*

Proof. Let X and Y be metric spaces (with metrics ρ_X and ρ_Y, respectively), and let $f : X \to Y$. We show the forward direction first. Suppose that f is continuous at a, and let $\{x_n\}$ be any sequence in X converging to a. Let $\epsilon > 0$ be given. Since f is continuous at a, there exists $\delta > 0$ such that

$$\rho_X(x, a) < \delta \quad \text{implies} \quad \rho_Y(f(x), f(a)) < \epsilon.$$

Since $\{x_n\}$ converges to a, for this δ, there exists $N \in \mathbb{N}$ such that

$$n > N \quad \text{implies} \quad \rho_X(x_n, a) < \delta.$$

Thus, for any $\epsilon > 0$, we have N such that, if $n > N$, then

$$\rho_X(x_n, a) < \delta, \quad \text{which implies} \quad \rho_Y(f(x_n), f(a)) < \epsilon.$$

Hence, $\{f(x_n)\}$ converges to $f(a)$.

Now we prove the backward direction. Suppose that f is not continuous at a. Negating Definition 2.3, this statement means that for some ϵ and for any δ, there exists $x \in X$ such that $\rho_X(x, a) < \delta$ and $\rho_Y(f(x), f(a)) \geq \epsilon$. For this ϵ and for each $\delta = \dfrac{1}{n}$, let x_n be the corresponding x. Then $\rho_X(x_n, a) < \dfrac{1}{n}$ and $\rho_Y(f(x_n), f(a)) \geq \epsilon$ for all n. That is, $\{x_n\}$ converges to a but $\{f(x_n)\}$ does not converge to $f(a)$. Hence, if f is not continuous, then the sequential condition is not satisfied. □

Definition 2.17. *A sequence $\{x_n\}$ in $\mathbb{R}$ is monotone increasing if $x_n \leq x_{n+1}$ for all n. Similarly, $\{x_n\}$ is monotone decreasing if $x_n \geq x_{n+1}$ for all n.*

Definition 2.18. *A sequence $\{x_n\}$ is bounded if there is a point a and a number $\delta > 0$ such that $\rho(x_n, a) \leq \delta$ for all n.*

Lemma 2.19. *A bounded monotone sequence in $\mathbb{R}$ is convergent.*

Proof. Consider the case where $\{x_n\}$ is monotone increasing and bounded above. (The case where $\{x_n\}$ is monotone decreasing and bounded below can be done similarly.) Let l be the least upper bound of the set $\{x_n \mid n \in \mathbb{N}\}$. That is, $x_n \leq l$ for all n, but for any $\epsilon > 0$, $l - \epsilon$ is not an upper bound, and so $l - \epsilon < x_N$ for some $N \in \mathbb{N}$. Then, if $n > N$, we have

$$l - \epsilon < x_N \leq x_n \leq l,$$

which implies $|x_n - l| < \epsilon$. In other words, $x_n \to l$ as $n \to \infty$, so $\{x_n\}$ is convergent. □

Lemma 2.20. *Any sequence in $\mathbb{R}$ has a monotone subsequence.*

Proof. Let $\{x_n\}$ be any sequence in $\mathbb{R}$. Call x_n a peak term if it is greater than or equal to all later terms. If there are infinitely many peak terms, then they obviously form a decreasing subsequence, and we are done. On the other hand, if there are only finitely many peak terms, then there is a last one x_{n_0} (or none at all), and then every later term is strictly less than some other later term. Therefore, in this case we can choose a strictly increasing subsequence. We have thus shown that any sequence $\{x_n\}$ in $\mathbb{R}$ has either a decreasing subsequence or a strictly increasing subsequence. □

Theorem 2.21. *Every bounded sequence in $\mathbb{R}$ has a convergent subsequence.*

Proof. Let $\{x_n\}$ be a bounded sequence in $\mathbb{R}$. Then, by Lemma 2.20, we can construct a monotone subsequence $\{x_{n_k}\}$ of $\{x_n\}$. Clearly, $\{x_{n_k}\}$ is bounded since $\{x_n\}$ is bounded. By Lemma 2.19, $\{x_{n_k}\}$ is convergent. Hence any sequence in $\mathbb{R}$ has a convergent subsequence. □

2.1.3 Completeness

Definition 2.22. *A sequence $\{x_n\}$ is a Cauchy sequence if for all $\epsilon > 0$, there exists $N \in \mathbb{N}$ such that $m, n > N$ implies $\rho(x_m, x_n) < \epsilon$.*

Lemma 2.23. *If $\{x_n\}$ is convergent, then $\{x_n\}$ is a Cauchy sequence.*

Proof. Let $\{x_n\}$ converge to a point a. Then, given $\epsilon > 0$, we can choose $N \in \mathbb{N}$ such that if $n > N$, then $\rho(x_n, a) < \dfrac{\epsilon}{2}$. Thus, for $m, n > N$, we have

$$\rho(x_m, x_n) \leq \rho(x_m, a) + \rho(a, x_n) < \frac{\epsilon}{2} + \frac{\epsilon}{2} = \epsilon.$$

Therefore, $\{x_n\}$ is a Cauchy sequence. □

Lemma 2.24. *If $\{x_n\}$ is Cauchy, and if a subsequence is convergent, then $\{x_n\}$ itself converges.*

Proof. Let $\{x_n\}$ be a Cauchy sequence and suppose that the subsequence $\{x_{n_k}\}$ converges to a point a as $k \to \infty$. Let $\epsilon > 0$ be given. Then, since $\{x_n\}$ is Cauchy, there exists N_1 such that $m, n > N_1$ implies $\rho(x_n, x_m) < \dfrac{\epsilon}{2}$. Also, since $\{x_{n_k}\}$ is convergent, there exists N_2 such that $k > N_2$ implies $\rho(x_{n_k}, a) < \dfrac{\epsilon}{2}$. Take $N = \max\{N_1, N_2\}$. Then for $m, k > N$ (and since $n_k \geq k > N$), we have

$$\rho(x_m, a) \leq \rho(x_m, x_{n_k}) + \rho(x_{n_k}, a) < \epsilon,$$

and so $\{x_m\}$ converges to a. □

Lemma 2.25. *If $\{x_n\}$ is a Cauchy sequence, then $\{x_n\}$ is bounded.*

Proof. Let $\{x_n\}$ be a Cauchy sequence. Then, for $\epsilon = 1$, there exists $N \in \mathbb{N}$ such that if $m, n > N$, then $\rho(x_m, x_n) < 1$. In particular, $N + 1 > N$, so $\rho(x_m, x_{N+1}) < 1$ for all $m > N$. Note that there are finitely many terms before x_N; accordingly, set
$K = \max\{\rho(x_{N+1}, x_1), \rho(x_{N+1}, x_2), \cdots, \rho(x_{N+1}, x_N)\}$. Then let $K' = \max\{1, K\}$. Then we have that $\rho(x_{N+1}, x_m) \leq K'$ for all m. Therefore, $\{x_n\}$ is bounded. □

Definition 2.26. *A metric space A is complete if every Cauchy sequence in A converges to a limit in A.*

Theorem 2.27. $\mathbb{R}$ *is complete.*

Proof. Let $\{x_n\}$ be a Cauchy sequence in $\mathbb{R}$. Then, by Lemma 2.25, $\{x_n\}$ is bounded, so by Theorem 2.21, $\{x_n\}$ has a convergent subsequence. Lemma 2.24 then implies that $\{x_n\}$ is convergent. □

2.1.4 The Contraction Mapping Fixed-Point Theorem

Definition 2.28. *A mapping K from a metric space X to itself is called a contraction if it is a Lipschitz mapping with constant less than 1; that is, if there is a constant C with $0 < C < 1$ such that $\rho(K(x), K(y)) \leq C\rho(x, y)$ for all $x, y \in X$.*

Definition 2.29. *Let K be a mapping from a metric space X to itself. A fixed point of K is a point x such that $K(x) = x$.*

Theorem 2.30. *(Fixed Point Theorem) Let X be a nonempty complete metric space and let $K : X \to X$ be a contraction. Then K has a unique fixed point.*

Proof. Let X be a nonempty complete metric space and let $K : X \to X$ be a contraction. Choose any x_0 in X and define the sequence $\{x_n\}_0^\infty$ inductively by setting $x_1 = K(x_0)$, $x_2 = K(x_1)$, $\cdots$, $x_n = K(x_{n-1})$. Set $\delta = \rho(x_1, x_0)$. We show by induction that, for all $n \in \mathbb{N}$, $\rho(x_{n+1}, x_n) \leq C^n\delta$. For the base step, we have

$$\rho(x_2, x_1) = \rho(K(x_1), K(x_0)) \leq C\rho(x_1, x_0) = C\delta,$$

so the claim is true for $n = 1$. Next, assume the claim is true for some $k \in \mathbb{N}$; that is, assume

$$\rho(x_{k+1}, x_k) \leq C^k\delta.$$

We have

$$\rho(x_{k+2}, x_{k+1}) = \rho(K(x_{k+1}), K(x_k)) \leq C\rho(x_{k+1}, x_k) \leq C \cdot C^k\delta = C^{k+1}\delta.$$

Thus, the claim is true for $k + 1$. Therefore, by induction, $\rho(x_{n+1}, x_n) \leq C^n\delta$ for all n. Next, let $m > n$. Then

$$\begin{aligned}\rho(x_m, x_n) &\leq \rho(x_n, x_{n+1}) + \rho(x_{n+1}, x_{n+2}) + \cdots + \rho(x_{m-1}, x_m) \\ &= \sum_{i=n}^{m-1} \rho(x_{i+1}, x_i) \leq \sum_{i=n}^{m-1} C^i\delta < \delta \sum_{i=n}^{\infty} C^i = C^n\delta \sum_{i=0}^{\infty} C^i = \frac{C^n\delta}{1 - C}.\end{aligned}$$

Noting that $C^n \to 0$ as $n \to \infty$ (since $C < 1$), it follows that $\{x_n\}$ is a Cauchy sequence. Since X is complete, $\{x_n\}$ converges to some a in X. Since K is Lipschitz, K is continuous, and so (by the sequential criterion)

$$K(a) = \lim_{n\to\infty} K(x_n) = \lim_{n\to\infty} x_{n+1} = a.$$

Thus, a is a fixed point for K.

Next, we claim that the fixed point of K is unique. Let x and y be fixed points of K. Then by Definition 2.29, $K(x) = x$ and $K(y) = y$. Additionally, by Definition 2.28, there exists a constant $0 < C < 1$ such that

$$\rho(x, y) = \rho(K(x), K(y)) \leq C\rho(x, y),$$

from which it follows that $(1-C)\rho(x, y) \leq 0$. Since $C < 1$, we must have $\rho(x, y) = 0$, which implies $x = y$. Therefore, the fixed point of a contraction is unique. □

2.1.5 The Picard-Lindelöf Theorem

Consider the ordinary differential equation

$$\frac{d\mathbf{x}}{dt} = f(\mathbf{x}), \quad \mathbf{x} \in \mathbb{R}^m.$$

Integrating both sides,

$$\mathbf{x}(t) = \mathbf{x}_0 + \int_{t_0}^{t} f(\mathbf{x}(s))ds.$$

Define a map $T : \mathbb{R}^m \to \mathbb{R}^m$ by

$$T(\mathbf{u}(t)) = \mathbf{x}_0 + \int_{t_0}^{t} f(\mathbf{u}(s))ds.$$

Suppose that $\mathbf{u}(t)$ is a fixed point of T; that is, suppose $T(\mathbf{u}(t)) = \mathbf{u}(t)$. It follows that

$$\mathbf{u}(t) = \mathbf{u}_0 + \int_{t_0}^{t} f(\mathbf{u}(s))ds,$$

or differentiating both sides

$$\frac{d\mathbf{u}}{dt} = f(\mathbf{u}).$$

Thus, $\mathbf{u}(t)$ is a fixed point of T if and only if it is a solution to the initial value problem.

Let $t_0, a, b \in \mathbb{R}$, let $J = [t_0 - a, t_0 + a]$, and let $\mathbf{x}(t)$ be a function from J to $\mathbb{R}^m$ with $\mathbf{x}(t_0) = \mathbf{x}_0$. Define $U = \overline{B}(\mathbf{x}_0, b)$ (the closed ball centered at $\mathbf{x}_0$ with radius b), and let $C^0(J, U)$ denote the set of continuous functions from J to U.

Theorem 2.31. *(Picard-Lindelöf Theorem) Consider the ordinary differential equation*

$$\frac{d\boldsymbol{x}}{dt} = f(\boldsymbol{x}), \quad \boldsymbol{x} \in \mathbb{R}^m,$$

with initial condition $\boldsymbol{x}(t_0) = \boldsymbol{x}_0$. Let $U = \overline{B}(\boldsymbol{x}_0, b)$ and $J = [t_0 - a, t_0 + a]$, where $f : U \to \mathbb{R}^m$ is Lipschitz with Lipschitz constant K, and $|f(\boldsymbol{x})| \leq M$ for all $\boldsymbol{x} \in U$. Then the initial value problem has a unique solution $\boldsymbol{x} \in C^0(J, U)$ as long as the time interval is chosen with a satisfying $0 < a < \min\left\{\frac{1}{K}, \frac{b}{M}\right\}$.

Proof. Define the function

$$T(\mathbf{u}(t)) = \mathbf{x}_0 + \int_{t_0}^{t} f(\mathbf{u}(s))ds.$$

Set $\mathbf{u}_0 = \mathbf{x}_0$ and let $\mathbf{u}_{n+1}(t) = T(\mathbf{u}_n(t))$. We must show that T is a contraction. First, since f is Lipschitz, f must be continuous. Since U is closed and bounded, it follows that f takes a maximum and a minimum on U. That is, there exists $M > 0$ such that $|f(\mathbf{x})| \leq M$ for all $\mathbf{x} \in U$. Next, note that

$$|T(\mathbf{u}(t)) - \mathbf{x}_0| = \left| \int_{t_0}^{t} f(\mathbf{u}(s))ds \right| \leq \left| \int_{t_0}^{t} |f(\mathbf{u}(s))|ds \right| \leq Ma.$$

Since $a < b/M$, $|T(\mathbf{u}(t)) - \mathbf{x}_0| < b$, which implies $T(\mathbf{u}(t)) \in \overline{B}(\mathbf{x}_0, b) = U$ for all $t \in J$. Hence, T maps $C^0(J, U)$ into itself.

Next, we show that T is a contraction. Let $u, v \in C^0(J, U)$. Then

$$\begin{aligned} |T(\mathbf{u}(t)) - T(\mathbf{v}(t))| &= \left| \int_{t_0}^{t} f(\mathbf{u}(s)) - f(\mathbf{v}(s))ds \right| \\ &\leq \int_{t_0}^{t} |f(\mathbf{u}(s)) - f(\mathbf{v}(s))|ds \\ &\leq K \int_{t_0}^{t} |\mathbf{u}(s) - \mathbf{v}(s)|ds \\ &\leq aK\rho(\mathbf{u}, \mathbf{v}). \end{aligned}$$

Hence, since $a < 1/K$, $aK < 1$. Therefore, T is a contraction. By the Contraction Mapping (Fixed Point) theorem, T has a unique fixed point. Therefore, the initial value problem has a unique solution. □

We may now apply the Picard-Lindelöf Theorem to our system. We have

$$\mathbf{x} = \begin{bmatrix} S \\ I \\ V \end{bmatrix}, \qquad f(\mathbf{x}) = \begin{bmatrix} \lambda - dS - kVS \\ kVS - \delta I \\ N_T \delta I - cV \end{bmatrix}.$$

Computing the Jacobian matrix then gives

$$\begin{bmatrix} -d - kV & 0 & -kS \\ kV & -\delta & kS \\ 0 & N_T\delta & -c \end{bmatrix},$$

where the partial derivatives of f exist and are continuous. It follows that f is Lipschitz continuous, so we are guaranteed a unique solution on some interval $[0, t^*]$.

2.2 Equilibria

An equilibrium is a set of values (S_0, I_0, V_0) such that if $S = S_0$, $I = I_0$, and $V = V_0$, then $\frac{dS}{dt}$, $\frac{dI}{dt}$, and $\frac{dV}{dt}$ are zero. That is, if the system is at equilibrium, then the values of S, I, and V will not

change. To find the equilibria for our system, we start with the following three equations:

$$\lambda - dS_0 - kV_0S_0 = 0, \tag{4}$$
$$kV_0S_0 - \delta I_0 = 0, \tag{5}$$
$$N_T\delta I_0 - cV_0 = 0. \tag{6}$$

Equation (6) implies

$$I_0 = \frac{c}{N_T\delta}V_0.$$

Substituting this value for I into Equation (5),

$$kV_0S_0 - \delta\left(\frac{c}{N_T\delta}\right)V_0 = 0,$$

or

$$V_0\left(kS_0 - \frac{c}{N_T}\right) = 0.$$

This implies $V_0 = 0$ or $S_0 = \dfrac{c}{N_Tk}$. For the first case, if $V_0 = 0$, then $I_0 = 0$ and $S_0 = \dfrac{\lambda}{d}$. On the other hand, if $S_0 = \dfrac{c}{N_Tk}$, then Equation (4) becomes

$$\lambda - d\left(\frac{c}{N_Tk}\right) - kV_0\left(\frac{c}{N_Tk}\right) = 0,$$

or

$$\frac{kc}{N_Tk}V_0 = \lambda - \frac{dc}{N_Tk},$$

and so

$$V_0 = \frac{N_T\lambda}{c} - \frac{d}{k}.$$

Accordingly,

$$I_0 = \frac{c}{N_T\delta}V_0 = \frac{c}{N_T\delta}\left(\frac{N_T\lambda}{c} - \frac{d}{k}\right),$$

or

$$I_0 = \frac{\lambda}{\delta} - \frac{dc}{N_T\delta k}.$$

In conclusion, we have two equilibria, E_1 and E_2, given in Table 2 and computed from the parameter values in Table 1. The first equilibrium is unstable, meaning solutions that start out near the equilibrium will move away from it. The second equilibrium is unstable, meaning solutions that start near the equilibrium stay near it. To verify this claim, consider the Jacobian matrix. Evaluated at the fist equilibrium, it becomes

$$\begin{bmatrix} -d & 0 & -\dfrac{k\lambda}{d} \\ 0 & -\delta & \dfrac{k\lambda}{d} \\ 0 & N_T\delta & -c \end{bmatrix},$$

	E_1		E_2	
S	λ/d	10	$c/N_T k$	0.6688
I	0	0	$\lambda/\delta - dc/N_T \delta k$	0.2793
V	0	0	$N_T \lambda/c - d/k$	128.8673

Table 2: Equilibria of SIV Model

which, according to MATLAB, has the eigenvalues

$$\begin{aligned}\lambda_1 &= -0.0109,\\ \lambda_2 &= 2.7697,\\ \lambda_3 &= -6.2097.\end{aligned}$$

Since one of the eigenvalues has a positive real part, the equilibrium is unstable. Now, evaluating the Jacobian at the second equilibrium gives

$$\begin{bmatrix} -\dfrac{N_T \lambda k}{c} & 0 & -\dfrac{c}{N_T} \\ \dfrac{N_T \lambda k}{c} - d & -\delta & \dfrac{c}{N_T} \\ 0 & N_T \delta & -c \end{bmatrix},$$

with the eigenvalues

$$\begin{aligned}\lambda_1 &= -0.0804 + 0.2184i,\\ \lambda_2 &= -0.0804 - 0.2184i,\\ \lambda_3 &= -3.4565.\end{aligned}$$

Since all eigenvalues have negative real parts, the second equilibrium is stable.

2.3 Analytical Solutions

One of the goals for this project was to find an analytical solution to the SIV model. Since finding a solution to the full system is a difficult task, we instead present analytical solutions to two simplified versions of the model, one including only the interaction and virus production terms, and another which introduces a death rate for the infected cells. Our two models are given by

$$\frac{dS}{dt} = -kVS, \tag{7}$$
$$\frac{dI}{dt} = kVS, \tag{8}$$
$$\frac{dV}{dt} = N_T \delta I, \tag{9}$$

and

$$\frac{dS}{dt} = -kVS, \tag{10}$$
$$\frac{dI}{dt} = kVS - \delta I, \tag{11}$$
$$\frac{dV}{dt} = N_T \delta I. \tag{12}$$

Below we briefly discuss the significance of each equation in the system.

First, examine (7). Note that there are no positive terms on the right hand side of the equation, so the number of susceptible cells must always be decreasing. The term kVS is the infection rate, or the rate at which healthy susceptible cells are converted into infected cells. This rate is proportional to the product of the virus particles and susceptible cells VS, with proportionality constant k. Next, examining (8), we see that dI/dt is always positive, so that the number of infected cells is increasing. In fact, I increases at the same rate that S decreases. Finally, note (9). The number of free virus particles V increases at a rate proportional to the number of infected cells I, with proportionality constant $N_T\delta$. The second system is nearly identical to the first. The only difference here is that we have added in the term $-\delta I$, representing the infected cell death rate.

These systems should show the same general trend as the full system early on in the course of the disease; namely, S decreases in time and I and V increase in time. Comparison of the three systems using numerical methods reveals that the approximations are not particularly accurate; nonetheless, solving the simplified models is a useful exercise and provides insight into the interactions of terms in the system.

2.3.1 Solution of the First Simplified Model

Recall that our first simplified version of the SIV model is given by

$$\frac{dS}{dt} = -kVS, \tag{13}$$

$$\frac{dI}{dt} = kVS, \tag{14}$$

$$\frac{dV}{dt} = N_T\delta I. \tag{15}$$

Before attempting to solve this system, we take a moment to verify that a unique solution exists. For our system,

$$y = \begin{bmatrix} S \\ I \\ V \end{bmatrix}, \qquad f(y) = \begin{bmatrix} -kVS \\ kVS \\ N_T\delta I \end{bmatrix},$$

where the system is said to be autonomous since it does not explicitly depend on the independent variable t. Computing the Jacobian matrix gives

$$J = \begin{bmatrix} -kV & 0 & -kS \\ kV & 0 & kS \\ 0 & N_T\delta & 0 \end{bmatrix},$$

where the partial derivatives of f exist and are continuous for any values of S, I, V, and t. It follows that f is Lipschitz continuous, and hence a unique solution exists on some interval $[0, t^*]$.

Having verified the existence of a unique solution, we are now ready to solve the system. First note

$$\frac{d}{dt}(S + I) = 0,$$

which implies

$$S + I = P, \tag{16}$$

where P is a constant determined by the initial conditions. It follows that

$$\frac{dV}{dt} = N_T\delta P - N_T\delta S.$$

Applying the chain rule,

$$\frac{dS}{dV} = \frac{dS/dt}{dV/dt} = -\frac{k}{N_T\delta}V\frac{S}{P-S},$$

separating variables and integrating,

$$P\ln|S| - S = -\frac{k}{2N_T\delta}V^2 + D.$$

Solving for V gives

$$V = \pm\sqrt{C - \frac{2N_T\delta P}{k}\ln|S| + \frac{2N_T\delta}{k}S}.$$

Here, C and D are constants determined by the initial conditions and related by $C = 2N_T\delta D/k$. To simplify, we assume that S and V are non-negative, yielding

$$V = \sqrt{C - \frac{2N_T\delta P}{k}\ln S + \frac{2N_T\delta}{k}S}. \tag{17}$$

Substituting this expression for V into the derivative for S gives

$$\frac{dS}{dt} = -k\left(\sqrt{C - \frac{2N_T\delta P}{k}\ln S + \frac{2N_T\delta}{k}S}\right)S.$$

Now, separating variables and integrating,

$$\int_{S_0}^{S}\frac{1}{\xi}\left(C - \frac{2N_T\delta P}{k}\ln\xi + \frac{2N_T\delta}{k}\xi\right)^{-1/2}d\xi = -k\int_{t_0}^{t}d\xi = -kt, \tag{18}$$

where we have set $t_0 = 0$. The integral above implicitly gives S as a function of t. I and V are then found from Equations (16) and (17), respectively. Under the initial conditions

$$S(0) = S_0, \qquad I(0) = I_0, \qquad V(0) = V_0,$$

the constants P and C are

$$P = S_0 + I_0 \qquad \text{and} \qquad C = V_0^2 + \frac{2N_T\delta P}{k}\ln S_0 - \frac{2N_T\delta}{k}S_0.$$

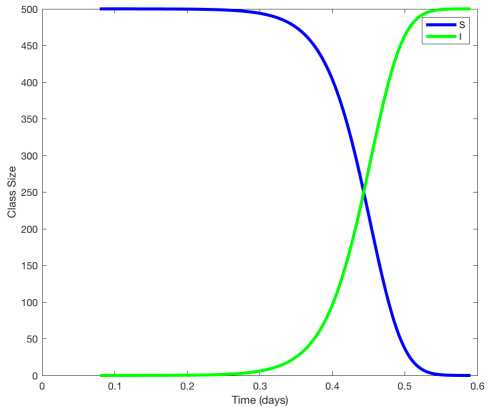


Figure 1: Plot of S and I (in number of cells per cubic milliliter) over time (in days).

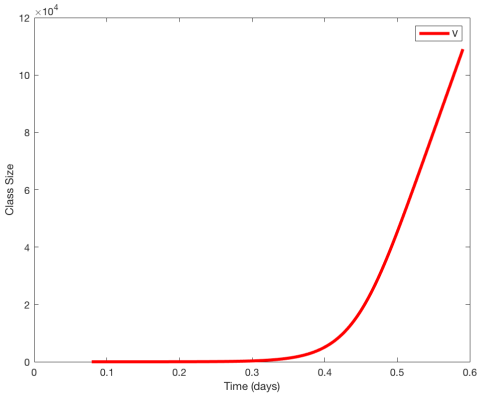


Figure 2: Plot of V (in number of virus particles per cubic milliliter) over time (in days).

Figures 1 and 2, created in MATLAB, give plots of the solution for the initial conditions $S(0) = 500$, $I(0) = 0$, and $V(0) = 0.1$. The plots were generated using the implicit analytical solution, under the assumption that S strictly decreases from its starting value to its equilibrium value.

2.3.2 Solution of the Second Simplified Model

Next, we introduce the δI term in Equation (14), giving our second version of the SIV model,

$$\frac{dS}{dt} = -kVS, \tag{19}$$

$$\frac{dI}{dt} = kVS - \delta I, \tag{20}$$

$$\frac{dV}{dt} = N_T \delta I, \tag{21}$$

with the initial conditions

$$S(0) = S_0, \qquad I(0) = I_0, \qquad V(0) = V_0.$$

Once again, we start by verifying the existence and uniqueness of a solution. Computing the Jacobian matrix for the second system gives

$$J = \begin{bmatrix} -kV & 0 & -kS \\ kV & -\delta & kS \\ 0 & N_T\delta & 0 \end{bmatrix}.$$

As before, the partial derivatives exist and are continuous for any S, I, V, and t. Therefore, a unique solution exists on $[0, t^*]$ for some $t^* \in \mathbb{R}$.

Having verified existence and uniqueness, we are now ready to solve the system. Firstly, note that

$$\frac{d}{dt}\left(S + I + \frac{V}{N_T}\right) = 0,$$

which implies

$$S + I + \frac{V}{N_T} = P, \tag{22}$$

where P is a constant determined by the initial conditions. In fact,

$$P = S_0 + I_0 + \frac{V_0}{N_T}.$$

Now, from Equation (22), we find

$$I = P - S - \frac{V}{N_T} \tag{23}$$

and

$$S = P - I - \frac{V}{N_T}. \tag{24}$$

Substituting for I in Equation (21), differentiating, and applying (23) and (24) gives

$$\frac{d^2V}{dt^2} = N_T\delta kPV - kV\frac{dV}{dt} - \delta kV^2 - \delta\frac{dV}{dt}.$$

Thus, we have reduced the system to a single differential equation,

$$V'' = N_T\delta kPV - kVV' - \delta kV^2 - \delta V', \tag{25}$$

where the prime indicates differentiation with respect to t. We next use a series of substitutions to bring (25) to a more easily solvable form. Using a transformation from [13], let

$$u = \frac{dt}{dV} = \frac{1}{V'}, \tag{26}$$

with the initial condition

$$u(V_0) = \frac{1}{N_T\delta I_0}.$$

Then we find

$$\frac{du}{dV} = (\delta k V^2 - N_T \delta k P V)u^3 + (kV + \delta)u^2. \tag{27}$$

Equation (27) is an Abel equation of the first kind; that is, it has the form

$$\frac{du}{dV} = f_3(V)u^3 + f_2(V)u^2 + f_1(V)u + f_0(V), \tag{28}$$

where in this case

$$\begin{aligned} f_3(V) &= \delta k V^2 - N_T \delta k P V, \\ f_2(V) &= kV + \delta, \\ f_1(V) &= 0, \\ f_0(V) &= 0. \end{aligned}$$

In [13], an iterative method is used to solve an equation of this type. Essentially, we obtain a sequence of approximate analytical solutions to the equation. The exact solution is given by the limit of the sequence at infinity. To start, let

$$\phi = \ln u, \tag{29}$$

or in other words,

$$u = e^{\phi}. \tag{30}$$

We then have the initial condition

$$\phi(V_0) = -\ln(N_T \delta I_0).$$

The differential equation then becomes

$$\frac{d\phi}{dV} = (\delta k V^2 - N_T \delta k P V)e^{2\phi} + (kV + \delta)e^{\phi}. \tag{31}$$

The expression e^{ϕ} can be expanded in a Taylor series as

$$e^{\phi} = \sum_{n=0}^{\infty} \frac{\phi^n}{n!} = 1 + \phi + \frac{\phi^2}{2} + \frac{\phi^3}{6} + \cdots,$$

so we may write (31) as

$$\begin{aligned} \frac{d\phi}{dV} =& (\delta k V^2 - N_T \delta k P V)\left(1 + 2\phi + \frac{(2\phi)^2}{2} + \cdots\right) \\ &+ (kV + \delta)\left(1 + \phi + \frac{\phi^2}{2} + \cdots\right). \end{aligned} \tag{32}$$

As a first approximation, $\phi_1(V)$, use only the first two terms of the Taylor series; that is, let

$$\begin{aligned} \frac{d\phi_1}{dV} &= (\delta k V^2 - N_T \delta k P V)(1 + 2\phi_1) + (kV + \delta)(1 + \phi_1) \\ &= \left[\delta k V^2 + (k - N_T \delta k P)V + \delta\right] + [2\delta k V^2 + (k - 2N_T \delta k P)V + \delta]\phi_1. \end{aligned} \tag{33}$$

The above is a first order, linear differential equation and can be solved with an integrating factor. Let

$$F = \exp\left[-\frac{2}{3}\delta k V^3 - \left(\frac{k}{2} - N_T \delta k P\right) V^2 - \delta V\right].$$

Then

$$\phi_1(V) = \frac{1}{F(V)}\left\{-\ln(N_T\delta I_0)F(V_0) + \int_{V_0}^{V} F(\xi)\left[\delta k\xi^2 + (k - N_T\delta kP)\xi + \delta\right] d\xi\right\}, \tag{34}$$

where we have taken $\phi_1(V_0) = \phi(V_0)$. Note that (32) can also be written as

$$\begin{aligned}\frac{d\phi}{dV} =&(\delta kV^2 - N_T\delta kPV)\left[1 + 2\phi + \sum_{n=2}^{\infty}\frac{(2\phi)^n}{n!}\right] \\ &+ (kV + \delta)\left[1 + \phi + \sum_{n=2}^{\infty}\frac{\phi^n}{n!}\right],\end{aligned}$$

or rearranging,

$$\begin{aligned}\frac{d\phi}{dV} =& \left[2\delta kV^2 + (k - 2N_T\delta kP)V + \delta\right]\phi + \left[\delta kV^2 + (k - N_T\delta kP)V + \delta\right] \\ &+ \sum_{n=2}^{\infty}\left[(\delta kV^2 - N_T\delta kPV)\frac{(2\phi)^n}{n!} + (kV + \delta)\frac{\phi^n}{n!}\right].\end{aligned}$$

For a second approximation, $\phi_2(V)$, plug into the infinite sum the expression for ϕ_1 obtained previously; that is, let

$$\begin{aligned}\frac{d\phi_2}{dV} =& \left[2\delta kV^2 + (k - 2N_T\delta kP)V + \delta\right]\phi_2 + \left[\delta kV^2 + (k - N_T\delta kP)V + \delta\right] \\ &+ \sum_{n=2}^{\infty}\left[(\delta kV^2 - N_T\delta kPV)\frac{(2\phi_1)^n}{n!} + (kV + \delta)\frac{\phi_1^n}{n!}\right].\end{aligned}$$

Just as before, the result is a first order, linear equation and can be solved with an integrating factor. The coefficient of ϕ_2 is the same as the coefficient of ϕ_1 in Equation (33), so we may use the same integrating factor. Thus,

$$\begin{aligned}\phi_2(V) =& -\frac{1}{F(V)}\ln(N_T\delta I_0)F(V_0) + \frac{1}{F(V)}\int_{V_0}^{V} F(\xi)\left[\delta k\xi^2 + (k - N_T\delta kP)\xi + \delta\right] d\xi \\ &+ \frac{1}{F(V)}\int_{V_0}^{V} F(\xi)\sum_{n=2}^{\infty}\left\{(\delta k\xi^2 - N_T\delta kP\xi)\frac{[2\phi_1(\xi)]^n}{n!} + (k\xi + \delta)\frac{[\phi_1(\xi)]^n}{n!}\right\} d\xi,\end{aligned}$$

where, as before, we have taken $\phi_2(V_0) = \phi(V_0)$. Continuing this process gives successively more accurate estimates for $\phi(V)$. In general, for any integer $m \geq 1$,

$$\begin{aligned}\phi_{m+1}(V) =& \frac{-1}{F(V)}\ln(N_T\delta I_0)F(V_0) + \frac{1}{F(V)}\int_{V_0}^{V} F(\xi)\left[\delta k\xi^2 + (k - N_T\delta kP)\xi + \delta\right] d\xi \\ &+ \frac{1}{F(V)}\int_{V_0}^{V} F(\xi)\sum_{n=2}^{\infty}\left\{(\delta k\xi^2 - N_T\delta kP\xi)\frac{[2\phi_m(\xi)]^n}{n!} + (k\xi + \delta)\frac{[\phi_m(\xi)]^n}{n!}\right\} d\xi,\end{aligned}$$

or in a more compact form,

$$\phi_{m+1}(V) = \phi_1(V) + \frac{1}{F(V)} \int_{V_0}^{V} F(\xi)(\delta k \xi^2 - N_T \delta k P \xi) \left[e^{2\phi_m(\xi)} - 1 - 2\phi_m(\xi) \right] d\xi + \frac{1}{F(V)} \int_{V_0}^{V} F(\xi)(k\xi + \delta) \left[e^{\phi_m(\xi)} - 1 - \phi_m(\xi) \right] d\xi.$$

In light of (34), this simplifies to

$$\begin{aligned} \phi_{m+1}(V) = &- \frac{\ln(N_T \delta I_0) F(V_0)}{F(V)} + \frac{\delta k}{F(V)} \int_{V_0}^{V} F(\xi)(\xi^2 - N_T P \xi) \left[e^{2\phi_m(\xi)} - 2\phi_m(\xi) \right] d\xi \\ &+ \frac{1}{F(V)} \int_{V_0}^{V} F(\xi)(k\xi + \delta) \left[e^{\phi_m(\xi)} - \phi_m(\xi) \right] d\xi. \end{aligned} \tag{35}$$

With each iteration, the approximation $\phi_m(V)$ should become closer to $\phi(V)$, the solution of (31); that is, $\lim_{m \to \infty} \phi_m(V) = \phi(V)$. Having outlined a method to obtain ϕ, we may now work backwards to find $V(t)$. By (30) and (26), we have

$$\frac{dt}{dV} = e^{\phi(V)},$$

or integrating both sides,

$$\int_{t_0}^{t} d\xi = \int_{V_0}^{V} e^{\phi(\xi)} d\xi.$$

Taking $t_0 = 0$, $V(t)$ is given implicitly by

$$t = \int_{V_0}^{V} e^{\phi(\xi)} d\xi. \tag{36}$$

Now, by Equation (19),

$$\frac{dS}{dt} = -kVS.$$

Separating variables and integrating,

$$\int_{S_0}^{S} \frac{1}{\xi} d\xi = -k \int_{t_0}^{t} V(\xi) d\xi,$$

which implies (for t_0=0)

$$S = S_0 \exp\left[-k \int_0^t V(\xi) d\xi \right]. \tag{37}$$

Finally, by (23),

$$I = P - S_0 \exp\left[-k \int_0^t V(\xi) d\xi \right] - \frac{V(t)}{N_T}. \tag{38}$$

This calculation completes the analytical solution of the second simplified model, with V given implicitly by (36) and S and I given in terms of V by (37) and (38), respectively.

Figures 3 and 4 give plots of the solution for the initial conditions $S(0) = 500$, $I(0) = 0$, $V(0) = 10$. As the analytical solution is computationally difficult to work with, Euler's method was used to create the plots.

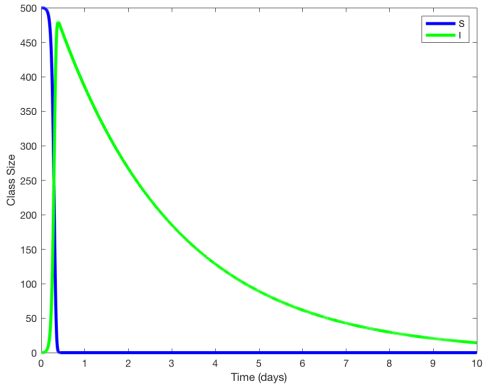


Figure 3: Plot of S and I (in number of cells per cubic milliliter) over time (in days) for the second model.

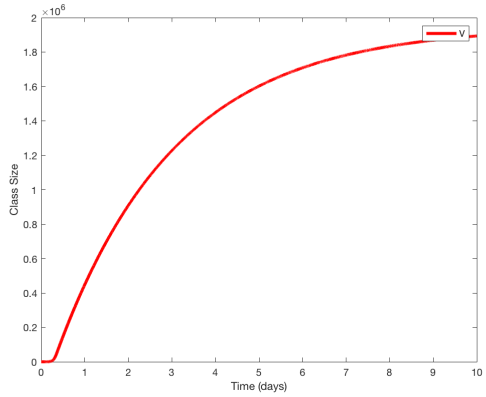


Figure 4: Plot of V (in number of virus particles per cubic milliliter) over time (in days) for the second model.

It is interesting to compare the results of the two models. Examining Figures 1, 2, 3, and 4, we see that the models start out similarly, with a level period followed by a sharp decrease in S and with sharp increases in I and V. One noticeable difference is that I experiences more moderate growth in the second model, which is to be expected since we have incorporated its death rate. The same can be said for V, whose increase depends on I. The long term behaviors of the models, on the other hand, are quite different. In both models, S eventually reaches the same equilibrium value of zero. Whereas in the first model, I eventually leveled off to a positive value (the same as the starting value for S), in the second, I eventually drops to zero. In the second model, rather than continuing to grow linearly as it does in the first, V eventually reaches an equilibrium value. This levelling occurs because there are no more infected cells to produce virus particles. To extend on this work, it would be interesting to next incorporate the viral clearance rate. This addition should give more realistic short term and long term outputs. On the whole, our two models give a great deal of insight into the roles of the infection term, virus production term, and infected cell death rate in the SIV model.

2.4 Numerical Solutions

Next, we apply several numerical methods to obtain an approximate solution to the SIV model.

2.4.1 Euler's Method

Euler's Method is the simplest technique in a collection called the Taylor Methods. It is easiest to understand graphically. To simplify matters, consider a single differential equation of the form

$$\frac{dy}{dt} = f(y,t),$$

with initial condition $y(t_0) = \alpha$. Starting at (t_0, α), Euler's Method approximates the solution $y(t)$ with a sequence N of short line segments, each of which has a slope determined by $f(t_i, y_i)$, $i = 1, 2, ...n$. Below we restate verbatim the algorithm for Euler's method given in [10].

ALGORITHM 2.32. *To approximate the solution of the initial-value problem*

$$y' = f(t,y), \qquad a \le t \le b, \qquad y(a) = \alpha,$$

at $(N+1)$ equally spaced numbers in the interval $[a,b]$:

INPUT *endpoints a, b; integer N; initial condition α.*
OUTPUT *approximation w to y at the $(N+1)$ values of t.*

Step 1 Set $h = (b-a)/N$;
$t = a$;
$w = \alpha$;
OUTPUT (t, w).
Step 2 For $i = 1, 2, \ldots, N$ do Steps 3,4.
Step 3 Set $w = w + hf(t,w)$; (Compute w_i.)
$t = a + ih$. (Compute t_i.)
Step 4 OUTPUT (t, w).
Step 5 STOP.

2.4.2 Higher Order Taylor Methods

As the step size h decreases (or as N increases), the approximation from Euler's method becomes more accurate. Alternatively, we can increase accuracy without changing the step size using Higher Order Taylor methods. As stated in [10], Taylor's Theorem says the following:

Theorem 2.33. *Suppose $f \in C^n[a,b]$, that $f^{(n+1)}$ exists on $[a,b]$, and $x_0 \in [a,b]$. For every $x \in [a,b]$, there exists a number $\xi(x)$ between x_0 and x with*

$$f(x) = P_n(x) + R_n(x),$$

where

$$\begin{aligned} P_n(x) =& f(x_0) + f'(x_0)(x-x_0) + \frac{f''(x_0)}{2!}(x-x_0)^2 + \cdots + \frac{f^{(n)}(x_0)}{n!}(x-x_0)^n \\ =& \sum_{k=0}^{n} \frac{f^{(k)}(x_0)}{k!}(x-x_0)^k \end{aligned}$$

and

$$R_n(x) = \frac{f^{(n+1)}(\xi(x))}{(n+1)!}(x - x_0)^{n+1}.$$

In Taylor's method of order n, we approximate the solution to the differential equation by considering only the P_n term. Notice that Euler's method is actually just Taylor's method of order 1. Below we provide an algorithm for the Taylor method of order n based on that given in [10].

ALGORITHM 2.34. *To approximate the solution of the initial-value problem*

$$y' = f(t, y), \qquad a \le t \le b, \qquad y(a) = \alpha,$$

at $(N + 1)$ equally spaced numbers in the interval $[a, b]$:

INPUT *endpoints a, b; integer N; initial condition α.*
OUTPUT *approximation w to y at the $(N + 1)$ values of t.*

Step 1 *Set $h = (b - a)/N$;*
$t = a$;
$w = \alpha$;
OUTPUT (t, w).
Step 2 *For $i = 1, 2, \ldots, N$ do Steps 3,4.*
Step 3 *Set $w = w + hT^{(n)}(t, w)$,*
$t = a + ih$,
where $T^{(n)}(t, w) = f(t, w) + \frac{h}{2}f'(t, w) + \cdots + \frac{h^{n-1}}{n!}f^{(n-1)}(t, w)$.
Step 4 *OUTPUT* (t, w).
Step 5 *STOP.*

Applying higher order Taylor methods is a bit more involved than applying Euler's method. As an example, let us use Taylor's method of order 2 to approximate the solution to the SIV model. Define functions $f_1(t)$, $f_2(t)$, and $f_3(t)$ as

$$f_1(t) = \frac{dS}{dt} = \lambda - dS - kVS, \tag{39}$$

$$f_2(t) = \frac{dI}{dt} = kVS - \delta I, \tag{40}$$

$$f_3(t) = \frac{dV}{dt} = N_T\delta I - cV. \tag{41}$$

By the Chain Rule, we have

$$\begin{aligned}\frac{df_1}{dt} &= \frac{\partial f_1}{\partial S}\frac{\partial S}{\partial t} + \frac{\partial f_1}{\partial I}\frac{\partial I}{\partial t} + \frac{\partial f_1}{\partial V}\frac{\partial V}{\partial t} \\ &= (-d - kV)(\lambda - dS - kVS) + (-kS)(N_T\delta I - cV),\end{aligned}$$

$$\begin{aligned}\frac{df_2}{dt} &= \frac{\partial f_2}{\partial S}\frac{\partial S}{\partial t} + \frac{\partial f_2}{\partial I}\frac{\partial I}{\partial t} + \frac{\partial f_2}{\partial V}\frac{\partial V}{\partial t} \\ &= (kV)(\lambda - dS - kVS) + (kS)(N_T\delta I - cV) + (-\delta)(kVS - \delta I),\end{aligned}$$

$$\begin{aligned}\frac{df_3}{dt} &= \frac{\partial f_3}{\partial S}\frac{\partial S}{\partial t} + \frac{\partial f_3}{\partial I}\frac{\partial I}{\partial t} + \frac{\partial f_3}{\partial V}\frac{\partial V}{\partial t} \\ &= (N_T\delta)(kVS - \delta I) + (-c)(N_T\delta I - cV).\end{aligned}$$

Consequently,

$$\begin{aligned}T_1^{(2)}(t,S,I,V) &= (\lambda - dS - kVS) + \frac{h}{2}\left[(-d-kV)(\lambda - dS - kVS) + (-kS)(N_T\delta I - cV)\right], \\ T_2^{(2)}(t,S,I,V) &= (kVS - \delta I) \\ &\quad + \frac{h}{2}\left[(kV)(\lambda - dS - kVS) + (kS)(N_T\delta I - cV) + (-\delta)(kVS - \delta I)\right], \\ T_3^{(2)}(t,S,I,V) &= (N_T\delta I - cV) + \frac{h}{2}\left[(N_T\delta)(kVS - \delta I) + (-c)(N_T\delta I - cV)\right],\end{aligned}$$

where $T_1^{(2)}$, $T_2^{(2)}$, and $T_3^{(2)}$ are the second-order Taylor polynomials for f_1, f_2, and f_3, respectively.

2.4.3 Runge-Kutta Methods

Taylor methods are easy to understand but cumbersome to use. Runge-Kutta methods have the advantage of converging quickly without requiring us to compute higher-order derivatives. As an example, we apply the Midpoint Method to the SIV model. The algorithm for the method is given below.

ALGORITHM 2.35. *To approximate the solution of the initial-value problem*

$$y' = f(t,y), \qquad a \le t \le b, \qquad y(a) = \alpha,$$

at $(N+1)$ equally spaced numbers in the interval $[a,b]$:

INPUT *endpoints a, b; integer N; initial condition α.*
OUTPUT *approximation w to y at the $(N+1)$ values of t.*

Step 1 *Set $h = (b-a)/N$;*
$t = a$;
$w = \alpha$;
OUTPUT (t,w).
Step 2 *For $i = 1,2,\ldots,N$ do Steps 3,4.*
Step 3 *Set $w = w + hf\left(t + \frac{h}{2}, w + \frac{h}{2}f(t,w)\right)$;*
$t = a + ih$.
Step 4 *OUTPUT (t,w).*
Step 5 *STOP.*

2.4.4 Graphs

Figures 5 and 6 shows a graph of the numerical approximation obtained from Euler's Method on the interval from $t = 0$ to $t = 200$, where time is given in days. (With a suitable step size, the other methods give similar results.) For the constants, we used the parameters given in Table 1. The initial conditions were $S(0) = 10$, $I(0) = 0$, and $V(0) = 0.1$. We used $N = 10,000$, giving a small step size of $h = 0.0002$. Notice how the solution approaches the stable equilibrium E_2 in Table 2.

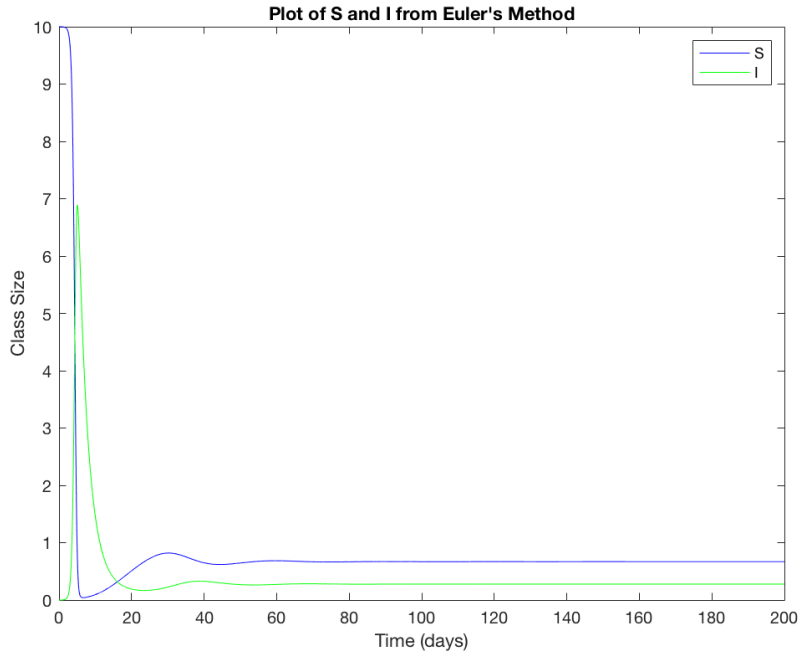


Figure 5: Approximate solution for S and I obtained from Euler's Method.

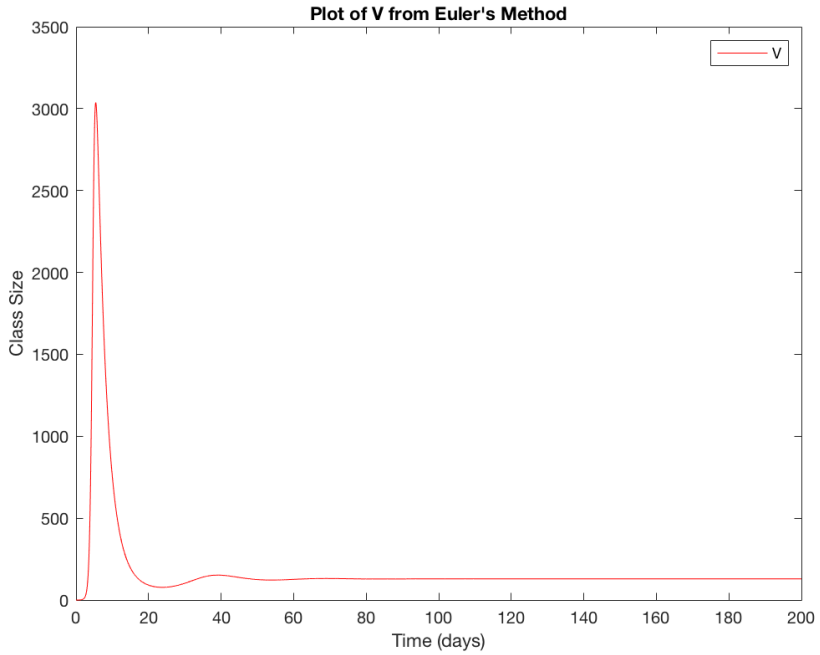


Figure 6: Approximate solution for V obtained from Euler's Method.

3 The Stochastic Model

3.1 Theory

3.1.1 Probability Spaces

Let Ω be a set. We will let Ω be our sample space, or the set of all possible outcomes of a random experiment.

Definition 3.1. *Let $\mathcal{A}$ be a collection of subsets of a set Ω. $\mathcal{A}$ is called a σ-algebra if*

(a) $\Omega \in \mathcal{A}$,

(b) $A^c \in \mathcal{A}$ *if* $A \in \mathcal{A}$, *where* $A^c = \Omega - A$,

(c) $\bigcup_{i=1}^{\infty} A_i \in \mathcal{A}$ *if* $A_1, A_2, \ldots \in \mathcal{A}$.

Note that if $\mathcal{A}$ is a σ-algebra, then $\emptyset \in \mathcal{A}$. Indeed, by part (a) of Definition 3.1, $\Omega \in \mathcal{A}$. Thus, by part (b), $\emptyset = \Omega - \Omega = \Omega^c \in \mathcal{A}$.

Also note that $\mathcal{A}$ is closed under countable intersections. Let $A_1, A_2, \ldots \in \mathcal{A}$. By part (b) of Definition 3.1, $A_1^c, A_2^c, \ldots \in \mathcal{A}$, so

$$\left(\bigcap_{i=1}^{\infty} A_i\right)^c = \bigcup_{i=1}^{\infty} A_i^c \in \mathcal{A},$$

where we have used part (c) of Definition 3.1 and DeMorgan's Law. Thus, by part (b) of Definition 3.1, $\bigcap_{i=1}^{\infty} A_i \in \mathcal{A}$.

Definition 3.2. *Let $P : \mathcal{A} \to [0,1]$ be a function, where $\mathcal{A}$ is a σ-algebra. P is called a probability measure if*

(a) $P(\Omega) = 1$,

(b) $P(A^c) = 1 - P(A)$ *for all* $A \in \mathcal{A}$,

(c) $P\left(\bigcup_{i=1}^{n} A_i\right) = \sum_{i=1}^{n} P(A_i)$ *if* $A_i \cap A_j = \emptyset$ *for* $i \neq j$.

Note that $P(\emptyset) = 0$. Indeed,

$$P(\emptyset) = P(\Omega^c) = 1 - P(\Omega) = 1 - 1 = 0.$$

Definition 3.3. *A triplet $(\Omega, \mathcal{A}, P)$ consisting of a sample space Ω, a σ-algebra $\mathcal{A}$ of subsets of Ω, and a probability measure P defined on $\mathcal{A}$ is called a probability space.*

Example 3.4. *Consider the random experiment of flipping a coin twice. We will label each outcome using two letters. For example, if the coin lands on heads for the first flip and tails for the second flip, the outcome would be called HT. Then the sample space is $\Omega = \{HH, HT, TH, TT\}$. Use the power set of $\mathcal{A}$ as the σ-algebra. Define a probability measure $P : \mathcal{A} \to [0,1]$ such that*

$$P(\{HH\}) = P(\{HT\}) = P(\{TH\}) = P(\{TT\}) = \frac{1}{4}.$$

Then $(\Omega, \mathcal{A}, P)$ is a probability space. As an example,

$$P(\{HH, TH\}) = P(\{HH\}) + P(\{TH\}) = \frac{1}{4} + \frac{1}{4} = \frac{1}{2}$$

is the probability of obtaining either two heads or tails followed by heads.

Example 3.5. *Consider the random experiment that involves choosing a number x from the interval $[0, 1]$. Then the sample space is $\Omega = [0, 1]$. Let the σ-algebra $\mathcal{A}$ be defined as the set generated by all intervals of the form $(a, b] \subset [0, 1]$. Define an event A to be $x \in (a, b]$, and define a probability measure $P : \mathcal{A} \to [0, 1]$ by $P(A) = b - a$. Then $(\Omega, \mathcal{A}, P)$ is a probability space.*

3.1.2 Random Variables

Let Ω be a sample space.

Definition 3.6. *A random variable is a function $X : \Omega \to \mathbb{R}$.*

Definition 3.7. *A random variable $X : \Omega \to \mathbb{R}$ is said to be measurable if*

$$A(x) = \{\omega \in \Omega : X(\omega) \leq x\} \in \mathcal{A} \text{ for all } x \in \mathbb{R}.$$

Definition 3.8. *Assume that X is a measurable. $F_X(x) = P(\{\omega \in \Omega : X(\omega) \leq x\})$ is called the distribution function or probability distribution of X.*

Note that for the distribution function F_X to be defined, X must be measurable since $\mathcal{A}$ is the domain of P.

Definition 3.9. *A random variable is called discrete if it takes values in a countable subset $\{x_1, x_2, x_3, \ldots\} \subset \mathbb{R}$. The probability mass function p of a discrete random variable X is the function $p : \{x_1, x_2, x_3, \ldots\} \to [0, 1]$ given by $p(x) = P(X = x) = P(\{\omega \in \Omega : X(\omega) = x\})$.*

Definition 3.10. *A random variable X is called continuous if there exists a piecewise continuous nonnegative function $p(x)$ such that $F_X(x) = \int_{-\infty}^{x} p(s)ds$. In this case, $p(x)$ is called the probability density function of X.*

Example 3.11. *Consider the random experiment of flipping a coin one time. The outcome will either be heads (H) or tails (T), so the sample space is $\Omega = \{H, T\}$. Then let $\mathcal{A} = \{\emptyset, \{H\}, \{T\}, \{H, T\}\}$, and define $P : \mathcal{A} \to [0, 1]$ by $P(\{H\}) = P(\{T\}) = \frac{1}{2}$. Define a random variable $X : \Omega \to \mathbb{R}$ by $X(T) = 0, X(H) = 5$. Our goal is to determine the probability distribution $F_X(x)$ and the probability mass function p. For $x < 0$,*

$$F_X(x) = P(\{\omega \in \Omega : X(\omega) \leq x < 0\}) = P(\emptyset) = 0.$$

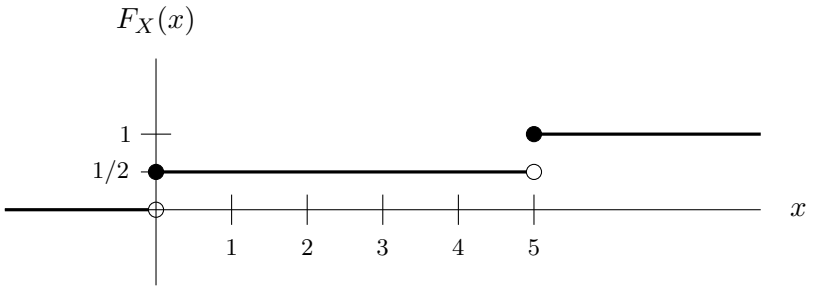
For $0 \leq x < 5$,

$$F_X(x) = P(\{\omega \in \Omega : X(\omega) \leq x\}) = P(\{T\}) = \frac{1}{2}.$$

For $x \geq 5$,

$$F_X(x) = P(\{\omega \in \Omega : X(\omega) \leq x\}) = P(\{T, H\}) = 1.$$

Graphically, we can depict F_X as follows:



The probability mass function $p : \{0, 5\} \to [0, 1]$ *is given by* $p(0) = \dfrac{1}{2}$, $p(5) = \dfrac{1}{2}$.

Example 3.12. *Consider the experiment of selecting a number* x *randomly from* $[0, 1]$. *Define the probability measure by* $P(A) = d - c$, *where* $A = \{x \in [0, 1] : c < x \leq d\}$. *Define the random variable* $X : [0, 1] \to \mathbb{R}$ *by* $X(x) = \exp(x)$. *Our goal is to find the distribution function and probability density function. First, note that for* $x < 1$,

$$F_X(x) = P\left(\{\omega \in [0, 1] : \exp(\omega) \leq x < 1\}\right) = P(\emptyset) = 0.$$

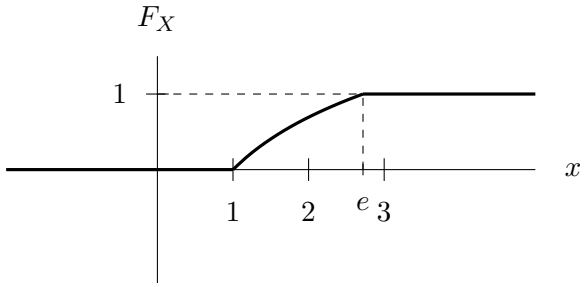
Similarly, for $1 \leq x \leq e$,

$$\begin{aligned} F_X(x) &= P\left(\{\omega \in [0, 1] : \exp(\omega) \leq x\}\right) \\ &= P\left(\{\omega \in [0, 1] : \omega \leq \ln x\}\right) \\ &= P\left([0, \ln x]\right) = \ln x. \end{aligned}$$

Finally, for $x > e$,

$$\begin{aligned} F_X(x) &= P\left(\{\omega \in [0, 1] : \exp(\omega) \leq x\}\right) \\ &= P\left(\{\omega \in [0, 1] : \omega \leq \ln x\}\right) \\ &= P\left([0, 1]\right) = 1. \end{aligned}$$

Plotting F_X *as a function of* x *gives the graph below.*



We can find the probability density function $p(x)$ *by differentiating* $F_X(x)$ *as follows. For* $x < 1$,

$$F_X'(x) = 0.$$

For $1 < x < e$,

$$F_X'(x) = \frac{d}{dx}(\ln x) = \frac{1}{x}.$$

Finally, for $x > e$,

$$F_X^{'} = 0.$$

Hence,

$$F_X = \int_{-\infty}^{x} p(s)ds,$$

where

$$p(s) = \begin{cases} 0, & s < 1 \\ \dfrac{1}{s}, & 1 \leq s \leq e \\ 0, & s > e \end{cases}.$$

3.1.3 Expectation

Suppose X is a discrete random variable, $X(\omega) \in \{x_1, x_2, \ldots\}$ for all $\omega \in \Omega$. Let $p(x)$ be the probability mass function for X; that is, $p(x) = P(X = x) = P(\{\omega \in \Omega : X(\omega) = x\})$.

Definition 3.13. *The expectation of X is defined as*

$$\mu = E(X) = \sum_i x_i p(x_i) = \sum_i X(\omega_i) P(\{\omega_i\}),$$

whenever the sum is convergent.

Definition 3.14. *Let X be a random variable and g be a function from $\mathbb{R}$ to $\mathbb{R}$. Then $Y = g(x)$ is also a random variable, and*

$$E(g(X)) = \sum_i g(x_i)p(x_i).$$

In particular, the k^{th} moment of X is

$$E(x^k) = \sum_i x_i^k p(x_i),$$

and the k^{th} central moment of X is defined as

$$E\left((X - \mu)^k\right) = \sum_i (x_i - \mu)^k p(x_i), \quad k = 1, 2, \ldots$$

Definition 3.15. *The variance of X is defined as the second central moment:*

$$Var(X) = E\left((X - \mu)^2\right).$$

Note that for $g, h : \mathbb{R} \to \mathbb{R}$ and $a, b \in \mathbb{R}$,

$$E\left(ag(X) + bh(X)\right) = aE(g(X)) + bE(h(X)).$$

It follows that $\text{Var}(X) = E\left((X-\mu)^2\right)$; indeed,

$$\begin{aligned}\text{Var}(X) = E\left((X-\mu)^2\right) &= \sum_i (x_i-\mu)^2 p(x_i) = \sum_i (x_i^2 - 2\mu x_i + \mu^2) p(x_i) \\ &= \sum_i x_i^2 p(x_i) - 2\mu \sum_i x_i p(x_i) + \mu^2 \sum_i p(x_i) \\ &= \sum_i x_i^2 p(x_i) - 2\mu^2 + \mu^2 = E(X^2) - \mu^2.\end{aligned}$$

Example 3.16. *Recall Example 3.11, the random experiment of flipping a coin one time. We have*

$$\begin{aligned}\mu = E(X) &= \sum_i X(\omega_i) P\left(\{\omega_i\}\right) \\ &= X(T) \cdot P\left(\{T\}\right) + X(H) \cdot P\left(\{H\}\right) \\ &= 0 \cdot \frac{1}{2} + 5 \cdot \frac{1}{2} = 2.5.\end{aligned}$$

Similarly,

$$\begin{aligned}E(X^2) &= \sum_i \left[X(\omega_i)\right]^2 P\left(\{\omega_i\}\right) \\ &= \left[X(T)\right]^2 \cdot P\left(\{T\}\right) + \left[X(H)\right]^2 \cdot P\left(\{H\}\right) \\ &= 0^2 \cdot \frac{1}{2} + 5^2 \cdot \frac{1}{2} = \frac{25}{2} = 12.5.\end{aligned}$$

Using the above results,

$$Var(X) = E(X^2) - \mu^2 = 12.5 - (2.5)^2 = 6.25.$$

Definition 3.17. *Suppose that X is a continuous random variable where $X(x) = x$ and with probability density $p(x)$. The expectation of X is defined as*

$$\mu = E(X) = \int_{-\infty}^{\infty} x p(x) dx.$$

The expectation of a function g of X is

$$E(g(x)) = \int_{-\infty}^{\infty} g(x) p(x) dx.$$

In particular, the k^{th} moment of X is

$$E(X^k) = \int_{-\infty}^{\infty} x^k p(x) dx,$$

while the k^{th} central moment is given by

$$E((X-\mu)^k) = \int_{-\infty}^{\infty} (x-\mu)^k p(x) dx.$$

The variance of X is defined as the second central moment:

$$Var(X) = E\left((X-\mu)^2\right).$$

Note that $\text{Var}(X) = E(X^2) - \mu^2$, as in the discrete case.

Example 3.18. *Recall Example 3.12, where a number x is randomly selected from $[0,1]$. We had $X(x) = \exp(x)$ and*

$$p(x) = \begin{cases} 0, & x < 1 \\ \dfrac{1}{x}, & 1 \le x \le e \\ 0, & x > e \end{cases}.$$

We have

$$\mu = E(X) = \int_{-\infty}^{\infty} \exp(x) p(x) dx = \int_1^e \frac{e^x}{x} dx \approx 6.3166,$$

and

$$E(X^2) = \int_1^e \frac{e^{2x}}{x} dx \approx 50.7610.$$

Using the above results,

$$Var(X) = 50.7610 - (6.3166)^2 = 10.8620.$$

Example 3.19. *Let $\Omega = \mathbb{R}$ and let $\mathcal{A}$ be a σ-algebra generated by integrals of the form $(a,b]$, that is, $(a,b] \in \mathcal{A}$ for any $a, b \in \mathbb{R}$ along with countable unions of such intervals and complements of the resulting sets. Define the random variable $X(x) = x$. Let $A \subset \mathcal{A}$ and let $\mu, \sigma \in \mathbb{R}$, $\sigma > 0$, be constants. Define*

$$P(A) = \int_A p(s) ds,$$

where

$$p(s) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left[-\frac{(s-\mu)^2}{2\sigma^2} \right].$$

That is,

$$P(a \le X \le b) = \int_a^b \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left[-\frac{(s-\mu)^2}{2\sigma^2} \right] ds.$$

X is said to be normally distributed with mean μ and variance σ^2 and it is denoted that $X \sim N(\mu, \sigma^2)$. Indeed, using Definition 3.17, it can be shown that $E(X) = \mu$ and $Var(X) = \sigma^2$.

3.1.4 Stochastic Processes

Definition 3.20. *A stochastic process is a family of random variables $\{X(t) : t \in \tau\}$ defined on a probability space $(\Omega, \mathcal{A}, P)$ and indexed by a parameter t, where t varies over a set τ. If τ is discrete, the stochastic process is called discrete. If τ is continuous, the stochastic process is called continuous.*

The parameter t usually plays the role of time, and the random variables can be discrete-valued or continuous-valued at each value of t. For a fixed value of ω, $X(t)$ is a called a sample path.

3.2 Expectation and Variance of a Solution

To convert our deterministic SIV model into a stochastic one, we replace the susceptible cell death rate d with a random variable. That is, rather than the system

$$\begin{aligned}\frac{dS}{dt} &= \lambda - dS - kVS,\\ \frac{dI}{dt} &= kVS - \delta I,\\ \frac{dV}{dt} &= Nt\delta I - cV,\end{aligned}$$

we solve the system

$$\frac{dS}{dt} = \lambda - d(\omega)S - kVS, \tag{42}$$

$$\frac{dI}{dt} = kVS - \delta I, \tag{43}$$

$$\frac{dV}{dt} = N_T\delta I - cV, \tag{44}$$

where $d(\omega)$ is a random variable. The analysis in [9] guarantees the existence of a unique solution to this new system.

For the random variable $d(\omega)$, we use 176 patient data values. The values are illustrated as a histogram in Figure 7. The probability distribution has the shape of exponential decay, peaking at small values and dropping off quickly as d increases.

Expectation values for S, I, and V over time were computed. These values are compared to the output of S, I, and V obtained from using the mean and median of d. Figures 8 through 10 give the resulting plots. Table 3 gives the expectation values and variances of the dependent variables at several points in time.

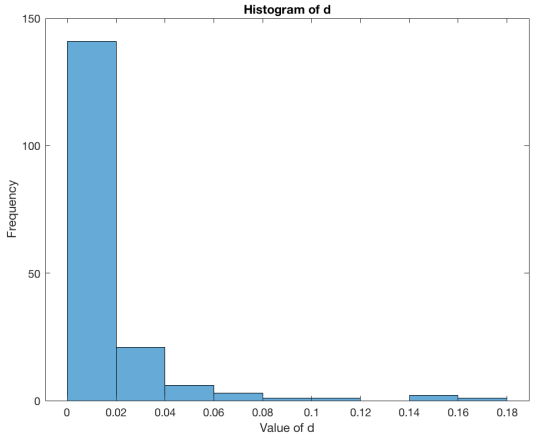


Figure 7: Histogram plot for the random variable $d(\omega)$.

t (days)	S_{avg}	S_{var}	I_{avg}	I_{var}	V_{avg}	V_{var}
4	6.3530	0.0284	3.0699	0.3563	864.0	2.73×10^4
8	0.0567	6.48×10^{-5}	2.6959	0.0189	1.40×10^3	5.49×10^3
12	0.1539	$1.67 \times 10 - 6$	0.7934	0.0013	405.2	338.7
16	0.3159	4.91×10^{-5}	0.3169	2.43×10^{-4}	156.8	57.2
20	0.5089	5.22×10^{-4}	0.1885	1.92×10^{-4}	90.04	40.5

Table 3: Expectation values and variances of S, I, and V at several points in time.

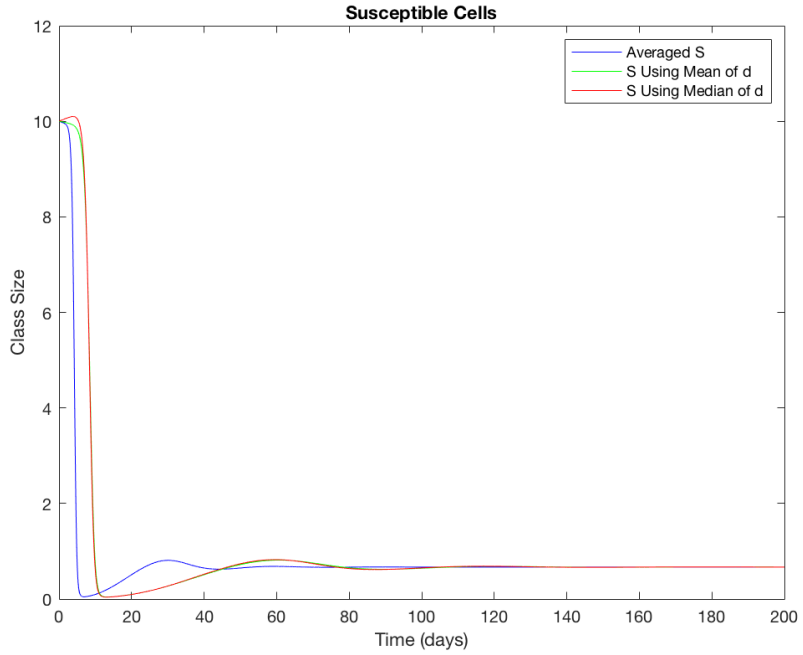


Figure 8: Comparison graph for S. The blue line gives the expectation value, obtained from computing S for each d and then averaging the results. The green and red lines were computed using the mean and median of d, respectively.

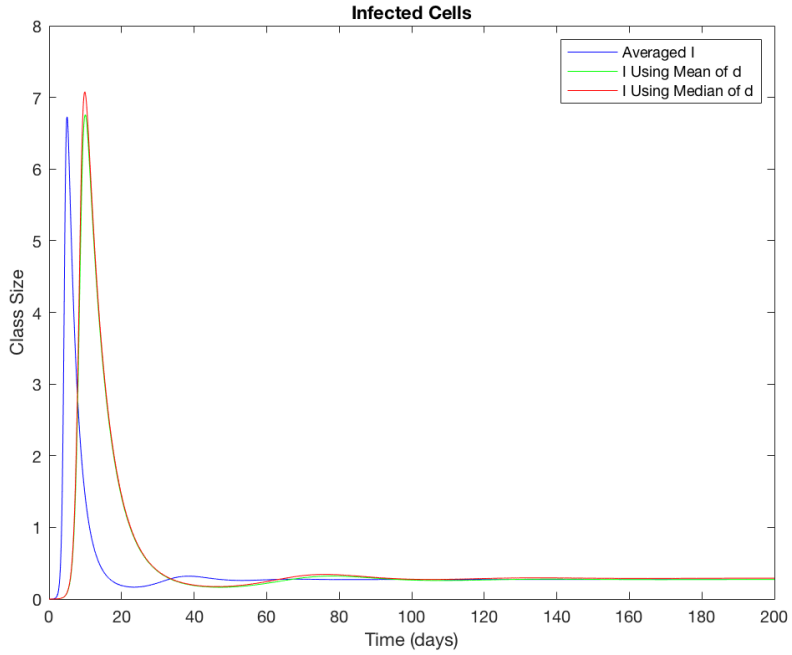


Figure 9: Comparison graph for I.

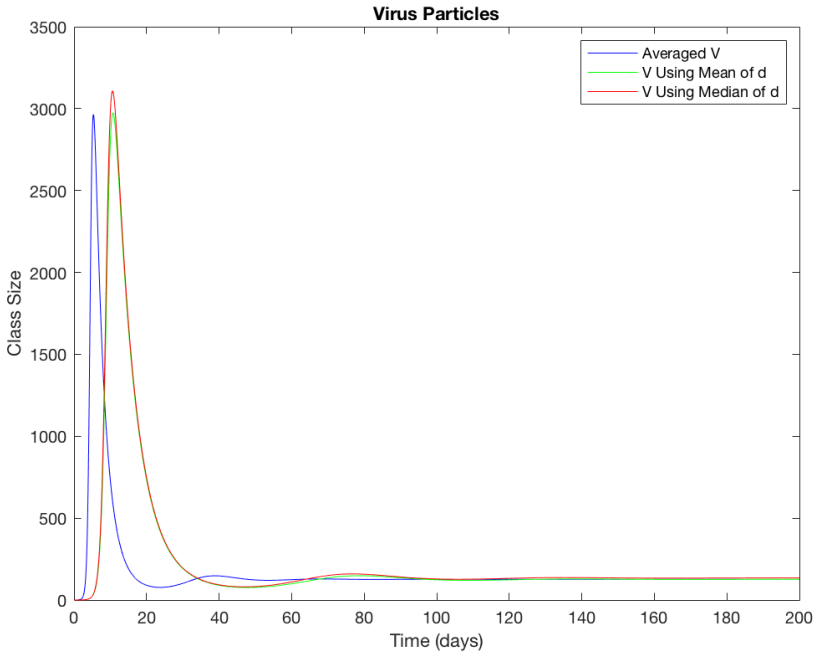


Figure 10: Comparison graph for V.

4 Conclusion

This section concludes our analysis of the SIV model as applied to HIV. We succeeded in obtaining analytical solutions to two simplified versions of the deterministic model. Although the predictions resulting from those simplifications were not particularly accurate, they gave insight into the roles of the infection rate, viral production rate, and infected cell death rate in the SIV model. Next, numerical methods allowed us to approximate solutions to the full SIV model, both the deterministic form, where all constants are known exactly, and its stochastic form, where the healthy cell death rate is represented by a random variable. In summary, the results demonstrate the progression of HIV in the absence of treatment and are made more realistic by the inclusion of randomness in the system.

5 Appendix of MATLAB Code

```
function [t,S,I,V] = HIV_euler(t_min,t_max,N,lambda,d,k,delta,Nt,c,S0,I0,V0)
h = (t_max - t_min)/N;
t = zeros(N+1,1);
S = zeros(N+1,1);
I = zeros(N+1,1);
V = zeros(N+1,1);
t(1) = t_min;
S(1) = S0;
I(1) = I0;
V(1) = V0;
for i = 1:N
    t(i+1) = t_min + i*h;
    S(i+1) = S(i) + h*(lambda - d*S(i) - k*V(i)*S(i));
    I(i+1) = I(i) + h*(k*V(i)*S(i)-delta*I(i));
    V(i+1) = V(i) + h*(Nt*delta*I(i)-c*V(i));
end
plot(t,S,'b')
hold on
plot(t,I,'g')
xlabel('Time (days)')
ylabel('Class Size')
legend('S','I')
title('Plot of S and I from Euler''s Method')
figure
plot(t,V,'r')
xlabel('Time (days)')
ylabel('Class Size')
legend('V')
title('Plot of V from Euler''s Method')
```

Figure 11: MATLAB code for Euler's Method.

```
function [t,S,I,V]=HIV_taylor2(t_min,t_max,N,lambda,d,k,delta,Nt,c,S0,I0,V0)
h = (t_max - t_min)/N;
t = zeros(N+1,1);
S = zeros(N+1,1);
I = zeros(N+1,1);
V = zeros(N+1,1);
t(1) = t_min;
S(1) = S0;
I(1) = I0;
V(1) = V0;
for i=1:N
    T_1=lambda-d*S(i)-k*V(i)*S(i)+h/2*(-
d*lambda+(d^2+k*d)*S(i)+(d*k+k^2+k*c)*V(i)*S(i)-k*lambda*V(i)-
k*Nt*delta*S(i)*I(i));
    T_2=k*V(i)*S(i)-delta*I(i)+h/2*(k*lambda*V(i)-k*d*S(i)-
k^2*(V(i))^2*S(i)+k*Nt*delta*S(i)*I(i)+(-k*c-
delta*k)*V(i)*S(i)+delta^2*I(i));
    T_3=Nt*delta*I(i)-c*V(i)+h/2*(Nt*delta*k*V(i)*S(i)+(-Nt*delta^2-
c*Nt*delta)*I(i)+c^2*V(i));
    t(i+1)=t_min+i*h;
    S(i+1)=S(i)+h*T_1;
    I(i+1)=I(i)+h*T_2;
    V(i+1)=V(i)+h*T_3;
end
```

Figure 12: MATLAB code for Taylor's Method of Order 2.

```
function [t,S,I,V] =
HIV_midpoint(t_min,t_max,N,lambda,d,k,delta,Nt,c,S0,I0,V0)
h = (t_max - t_min)/N;
t = zeros(N+1,1);
S = zeros(N+1,1);
I = zeros(N+1,1);
V = zeros(N+1,1);
t(1) = t_min;
S(1) = S0;
I(1) = I0;
V(1) = V0;
for i = 1:N
    t(i+1) = t_min + i*h;
    S(i+1) = S(i) + h*(lambda-d*(S(i)+h*lambda/2-h*d/2*S(i)-h*k/2*V(i)*S(i))-
k*(V(i)+h*Nt*delta/2*I(i)-h*c/2*V(i))*(S(i)+h*lambda/2-h*d/2*S(i)-
h*k/2*V(i)*S(i)));
    I(i+1) = I(i) + h*(k*(V(i)+h*Nt*delta/2*I(i)-
h*c/2*V(i))*(S(i)+h*lambda/2-h*d/2*S(i)-h*k/2*V(i)*S(i))-
delta*(I(i)+h*k/2*V(i)*S(i)-h*delta/2*I(i)));
    V(i+1) = V(i) + h*(Nt*delta*(I(i)+h*k/2*V(i)*S(i)-h*delta/2*I(i))-
c*(V(i)+h*Nt*delta/2*I(i)-h*c/2*V(i)));
end
```

Figure 13: MATLAB code for the Midpoint Method.

```
function [t,S,I,V] =
HIV_RungeKutta4(t_min,t_max,N,lambda,d,k,delta,Nt,c,S0,I0,V0)
h = (t_max - t_min)/N;
t = zeros(N+1,1);
S = zeros(N+1,1);
I = zeros(N+1,1);
V = zeros(N+1,1);
t(1) = t_min;
S(1) = S0;
I(1) = I0;
V(1) = V0;
for i = 1:N
    t(i+1) = t_min + i*h;
    kS1=h*(lambda-d*S(i)-k*V(i)*S(i));
    kI1=h*(k*V(i)*S(i)-delta*I(i));
    kV1=h*(Nt*delta*I(i)-c*V(i));
    kS2=h*(lambda-d*(S(i)+1/2*kS1)-k*(V(i)+1/2*kV1)*(S(i)+1/2*kS1));
    kI2=h*(k*(V(i)+1/2*kV1)*(S(i)+1/2*kS1)-delta*(I(i)+1/2*kI1));
    kV2=h*(Nt*delta*(I(i)+1/2*kI1)-c*(V(i)+1/2*kV1));
    kS3=h*(lambda-d*(S(i)+1/2*kS2)-k*(V(i)+1/2*kV2)*(S(i)+1/2*kS2));
    kI3=h*(k*(V(i)+1/2*kV2)*(S(i)+1/2*kS2)-delta*(I(i)+1/2*kI2));
    kV3=h*(Nt*delta*(I(i)+1/2*kI2)-c*(V(i)+1/2*kV2));
    kS4=h*(lambda-d*(S(i)+kS3)-k*(V(i)+kV3)*(S(i)+kS3));
    kI4=h*(k*(V(i)+kV3)*(S(i)+kS3)-delta*(I(i)+kI3));
    kV4=h*(Nt*delta*(I(i)+kI3)-c*(V(i)+kV3));
    S(i+1) = S(i)+1/6*(kS1+2*kS2+2*kS3+kS4);
    I(i+1) = I(i)+1/6*(kI1+2*kI2+2*kI3+kI4);
    V(i+1) = V(i)+1/6*(kV1+2*kV2+2*kV3+kV4);
end
```

Figure 14: MATLAB code for the Runge-Kutta Method of Order 4.

```
% Stochastic_Comparison_Graph_170
% Uses 176 data values for d
d=[8.321*10^(-14),2.657*10^(-10),6.955*10^(-08),1.360*10^(-06),7.955*10^(-05),1.350*10^(-
04),4.462*10^(-04),4.713*10^(-04),4.762*10^(-04),8.821*10^(-04),9.397*10^(-04),9.898*10^(-
04),1.342*10^(-03),1.395*10^(-03),1.396*10^(-03),1.405*10^(-03),1.437*10^(-03),1.441*10^(-
03),1.559*10^(-03),1.582*10^(-03),1.640*10^(-03),1.807*10^(-03),1.813*10^(-03),1.814*10^(-
03),2.067*10^(-03),2.082*10^(-03),2.311*10^(-03),2.483*10^(-03),2.602*10^(-03),2.634*10^(-
03),2.972*10^(-03),2.992*10^(-03),3.331*10^(-03),3.343*10^(-03),3.353*10^(-03),3.438*10^(-
03),3.858*10^(-03),4.094*10^(-03),4.393*10^(-03),4.481*10^(-03),4.629*10^(-03),4.917*10^(-
03),5.242*10^(-03),6.688*10^(-03),7.322*10^(-03),7.692*10^(-03),9.250*10^(-03),9.547*10^(-
03),9.604*10^(-03),9.966*10^(-03),1.024*10^(-02),1.040*10^(-02),1.057*10^(-02),1.088*10^(-
02),1.095*10^(-02),1.166*10^(-02),1.249*10^(-02),1.286*10^(-02),1.287*10^(-02),1.297*10^(-
02),1.325*10^(-02),1.379*10^(-02),1.463*10^(-02),1.555*10^(-02),1.594*10^(-02),1.663*10^(-
02),1.700*10^(-02),1.724*10^(-02),1.893*10^(-02),1.994*10^(-02),2.016*10^(-02),2.049*10^(-
02),2.239*10^(-02),2.272*10^(-02),2.468*10^(-02),2.629*10^(-02),2.675*10^(-02),3.318*10^(-
02),3.547*10^(-02),3.622*10^(-02),3.728*10^(-02),4.207*10^(-02),4.349*10^(-02),4.371*10^(-
02),5.074*10^(-02),6.060*10^(-02),6.916*10^(-02),8.688*10^(-02),1.695*10^(-01),3.925*10^(-
02),3.917*10^(-03),3.004*10^(-04),1.902*10^(-02),6.698*10^(-04),1.452*10^(-03),7.108*10^(-
03),1.407*10^(-02),1.193*10^(-02),1.064*10^(-03),1.258*10^(-03),3.889*10^(-02),1.277*10^(-
03),1.288*10^(-03),6.809*10^(-04),5.433*10^(-03),3.163*10^(-02),2.190*10^(-03),1.972*10^(-
04),2.314*10^(-02),5.624*10^(-04),2.752*10^(-03),3.557*10^(-03),2.119*10^(-02),1.014*10^(-
03),6.196*10^(-04),1.083*10^(-03),9.985*10^(-03),1.307*10^(-02),1.085*10^(-01),9.022*10^(-
03),2.344*10^(-06),1.283*10^(-03),1.018*10^(-03),1.068*10^(-03),4.147*10^(-02),7.700*10^(-
03),7.113*10^(-02),8.259*10^(-03),3.423*10^(-02),9.073*10^(-04),4.722*10^(-04),4.762*10^(-
03),2.776*10^(-03),4.468*10^(-03),3.890*10^(-04),4.910*10^(-03),1.341*10^(-03),4.411*10^(-
02),5.382*10^(-03),1.970*10^(-03),4.640*10^(-04),1.345*10^(-03),8.360*10^(-03),9.590*10^(-
04),1.645*10^(-04),2.576*10^(-02),9.921*10^(-03),1.980*10^(-03),4.136*10^(-03),2.456*10^(-
02),3.923*10^(-02),1.105*10^(-03),1.399*10^(-02),1.671*10^(-06),1.319*10^(-03),2.012*10^(-
03),5.157*10^(-04),1.565*10^(-02),1.096*10^(-02),2.945*10^(-04),4.589*10^(-06),1.403*10^(-
01),3.993*10^(-03),8.774*10^(-03),6.315*10^(-03),5.208*10^(-03),4.218*10^(-03),9.837*10^(-
04),2.315*10^(-02),1.783*10^(-02),1.376*10^(-04),1.307*10^(-03),8.058*10^(-04),1.328*10^(-
03),4.022*10^(-03),1.403*10^(-01)];

% Compute average values and variances for S, I, and V using each d value
Smat=zeros(176,10001);
Imat=zeros(176,10001);
Vmat=zeros(176,10001);
N=10000;
for i=1:176
[t,S,I,V]=HIV_RungeKutta4(0,200,10000,0.1089,d(i),0.001179,0.3660,1426.8/0.3660,3.074,10,0,0.1);
Smat(i,:)=S;
Imat(i,:)=I;
Vmat(i,:)=V;
end
Savg=zeros(10001,1);
Iavg=zeros(10001,1);
Vavg=zeros(10001,1);
for i=1:10001
Savg(i)=mean(Smat(:,i));
Iavg(i)=mean(Imat(:,i));
Vavg(i)=mean(Vmat(:,i));
end
Svar=zeros(10001,1);
Ivar=zeros(10001,1);
Vvar=zeros(10001,1);
for i=1:10001
Svar(i)=var(Smat(:,i));
Ivar(i)=var(Imat(:,i));
Vvar(i)=var(Vmat(:,i));
end

 % Use mean of d to compute S, I, and V

 [tm,Sm,Im,Vm]=HIV_RungeKutta4(0,100,N,0.1089,mean(d),0.001179,0.3660,3898.360656,3.074,10,0,0.1);

 % Use median of d to compute S, I, and V

 [tmed,Smed,Imed,Vmed]=HIV_RungeKutta4(0,100,N,0.1089,median(d),0.001179,0.3660,3898.360656,3.074,10
 ,0,0.1);

 % Plot Solutions for Comparison

 plot(t,Savg,'b')
 hold on
 plot(t,Sm,'g')
 hold on
 plot(t,Smed,'r')
 xlabel('Time (days)')
 ylabel('Class Size')
 title('Susceptible Cells')
 legend('Averaged S','S Using Means of d','S Using Median of d')

 figure
 plot(t,Iavg,'b')
 hold on
 plot(t,Im,'g')
 hold on
 plot(t,Imed,'r')
 xlabel('Time (days)')
 ylabel('Class Size')
 title('Infected Cells')
 legend('Averaged I','I Using Means of d','I Using Median of d')

 figure
 plot(t,Vavg,'b')
 hold on
 plot(t,Vm,'g')
 hold on
 plot(t,Vmed,'r')
 xlabel('Time (days)')
 ylabel('Class Size')
 title('Virus Particles')
 legend('Averaged V','V Using Means of d','V Using Median of d')
```

Figure 15: MATLAB code used to compute and plot the expectation values and variances of S, I, and V.

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